For Deleval please

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SEARCH REQUEST FORM

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Scientific and Technical Information Center

Requester's Full Name: SABINA GRUPP Examiner #: 74141 Date: 11/12/03
Art Unit: 1616 Phone Number 305-3910 Serial Number: 10/069,414
Mail Box and Bldg/Room Location: 2D19 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Agents for the enhanced oxygen delivery - amended

Inventors (please provide full names): Lehn Jean-Marie

Earliest Priority Filing Date: 8/25/~~98~~ 1999 371 of PCT/US00/22583 8/17/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Cl -11

Please search for the compds BGSC + BGTC, structures of which are on p-18 (enclosed)

You may leave open at C-17 for broader search, after searching separately BGSC + BGTC

Please see attached sheet

Thank you

STAFF USE ONLY

Searcher: [illegible]
Searcher Phone #: 4498
Searcher Location:
Date Searcher Picked Up: 12/8
Date Completed: 12/8
Searcher Prep & Review Time:
Clerical Prep Time: 10
Online Time: +15

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 16:55:58 ON 08 DEC 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    7 DEC 2003  HIGHEST RN 624286-58-4
DICTIONARY FILE UPDATES:   7 DEC 2003  HIGHEST RN 624286-58-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L17             STR
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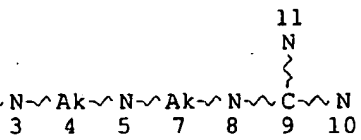


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  11

STEREO ATTRIBUTES: NONE
L19       35097 SEA FILE=REGISTRY SSS FUL L17

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SEARCH TIME: 00.00.13

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               SEL RN

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L26             773 S E4-E11,E14
                E NICOLAU Y/AU
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                E GMP/PA,CS
L28              89 S E3-E39
L29               6 S L25 AND L26-L28
L30              10 S L25,L29
L31               1 S L30 AND L8
L32               1 S L30 AND L12
L33               1 S L31,L32
L34              10 S L30-L33

     FILE 'USPATFULL, USPAT2' ENTERED AT 16:55:43 ON 08 DEC 2003
L35               5 S L7

     FILE 'REGISTRY' ENTERED AT 16:55:58 ON 08 DEC 2003

=> d ide can tot l7

L7   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   182056-15-1  REGISTRY
CN   Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]ami
     no]ethyl]carbamate, dihydrochloride (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C36 H66 N8 O2 . 2 Cl H
SR   CA
LC   STN Files:  CA, CAPLUS, USPATFULL
CRN  (182056-06-0)

Absolute stereochemistry.
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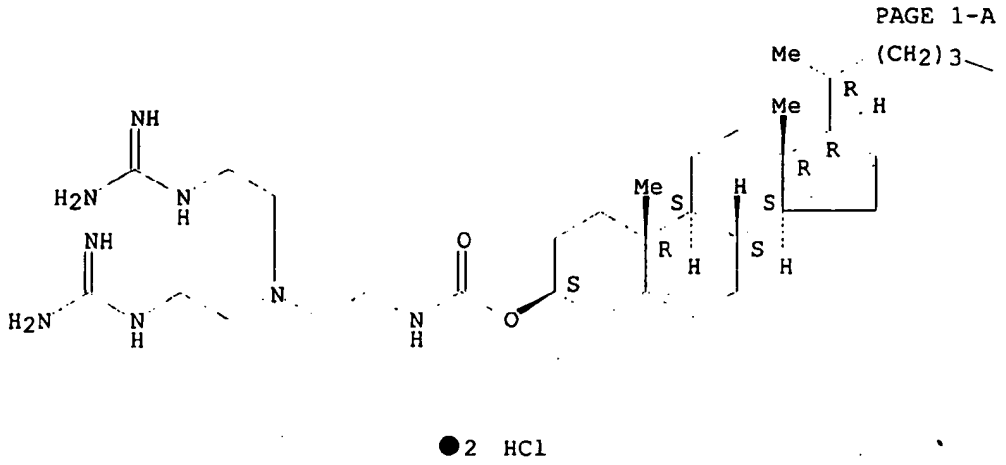


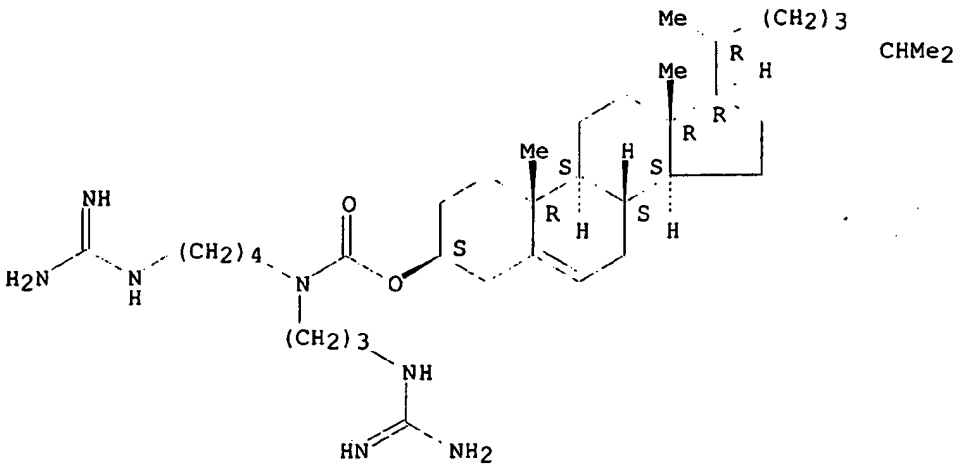
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:234484

REFERENCE 2: 125:239451

L7 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 182056-12-8 REGISTRY
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H67 N7 O2 . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (182055-89-6)

Absolute stereochemistry.



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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

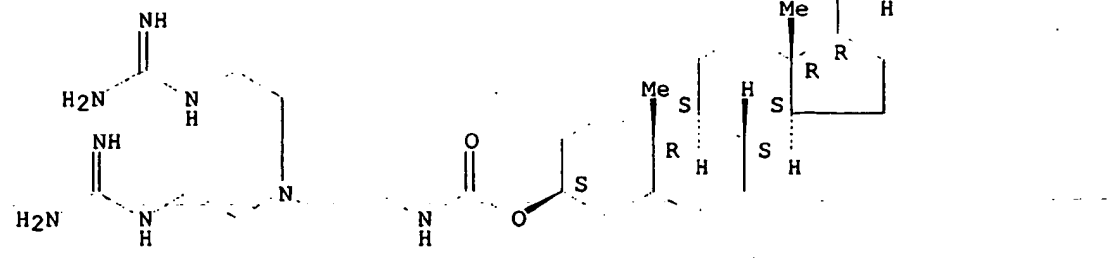
REFERENCE 1: 127:234484

REFERENCE 2: 125:239451

L7 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN **182056-06-0** REGISTRY
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C36 H66 N8 O2**
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:255843

REFERENCE 2: 137:389091

REFERENCE 3: 136:319345

REFERENCE 4: 134:212794

REFERENCE 5: 131:106801

REFERENCE 6: 131:54460

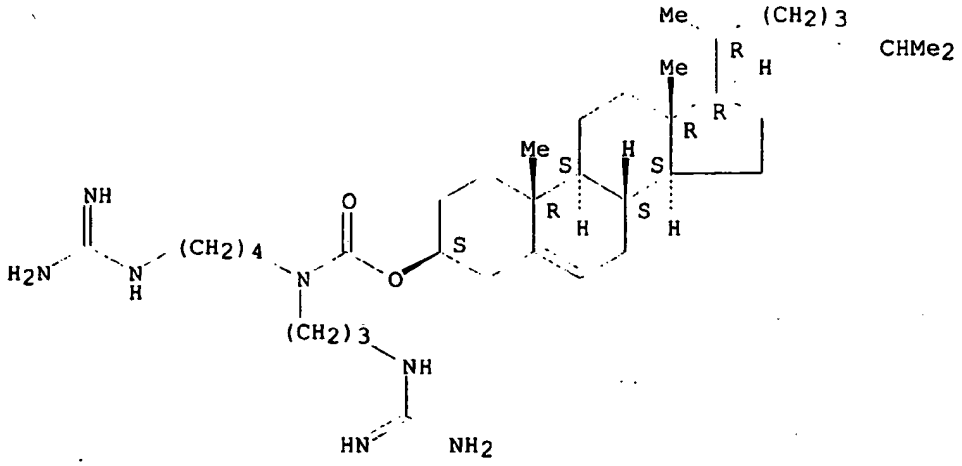
REFERENCE 7: 130:57047

REFERENCE 8: 126:258428

REFERENCE 9: 125:239451

L7 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN **182055-89-6** REGISTRY
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C37 H67 N7 O2**
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



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REFERENCE 1: 134:212794

REFERENCE 2: 125:239451

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CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 16:56:21 ON 08 DEC 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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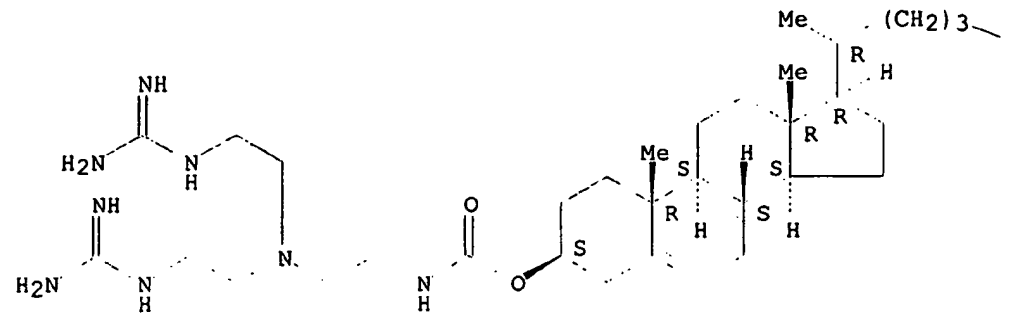
L35 ANSWER 1 OF 5 USPATFULL on STN
AN 2002:88021 USPATFULL
TI Stabilization of lipid:DNA formulations during nebulization
IN Densmore, Jr., Charles L., The Woodlands, TX, United States
Knight, J. Vernon, Houston, TX, United States
Waldrep, J. Clifford, The Woodlands, TX, United States
Kinsey, Berma M., Houston, TX, United States
PA Research Development Foundation, Carson City, NV, United States (U.S. corporation)
PI US 6375980 B1 20020423
AI US 1999-356635 19990719 (9)
RLI Continuation-in-part of Ser. No. US 1999-227648, filed on 8 Jan 1999, now patented, Pat. No. US 6106859, issued on 22 Aug 2000
PRAI US 1998-71052P 19980108 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Schwartzman, Robert A.; Assistant Examiner: Schnizer, Richard
LREP Adler, Benjamin Aaron
CLMN Number of Claims: 9
ECL Exemplary Claim: 4
DRWN 22 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 1140
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, a neutral co-lipid; and tryptone. Also provided is a nebulized cationic lipid: neutral co-lipid: DNA suspension useful for lipid-DNA transfections, wherein the cationic lipid is bis(guanidinium)-tren-cholesterol and the neutral co-lipid is dioleoylphosphatidylethanolamine (DOPE).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **182056-06-0**
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)
RN 182056-06-0 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



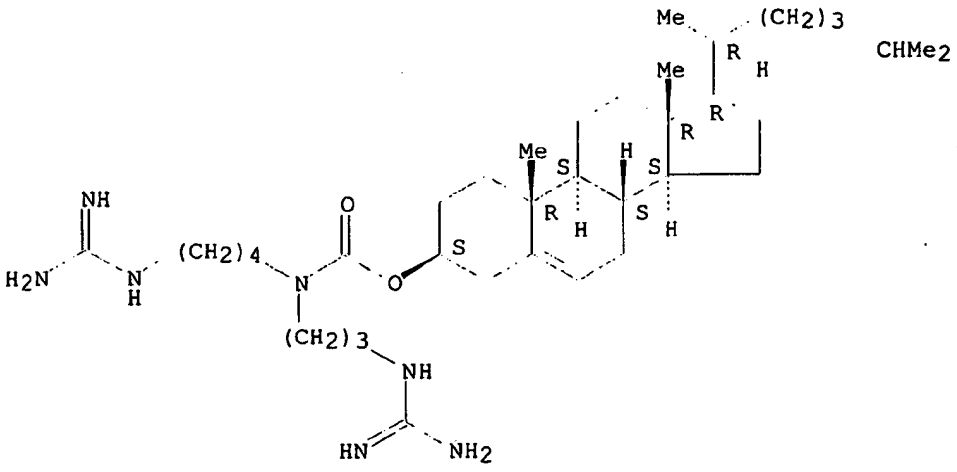
PAGE 1-B

CHMe2

L35 ANSWER 2 OF 5 USPATFULL on STN
AN 2001:202605 USPATFULL
TI Compounds related to the amidinium family, pharmaceutical compositions containing same, and uses thereof
IN Lehn, Jean-Marie, Strasbourg, France
Lehn, Pierre, Paris, France
Vigneron, Jean-Pierre, Boissy-sur-Saint-Yon, France
PA Centre National de la Recherche Scientifique, Paris, France (non-U.S. corporation)
PI US 6316422 B1 20011113
AI US 2000-706619 20001106 (9)
RLI Continuation of Ser. No. US 125825, now patented, Pat. No. US 6143729
PRAI FR 1996-2604 19960301
FR 1996-9557 19960730
DT Utility
FS GRANTED
EXNAM Primary Examiner: LeGuyader, John L.; Assistant Examiner: Epps, Janet L.
LREP Synnestvedt & Lechner LLP
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 959
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel amidinium derivatives of formula (I), wherein R1 is a cholesterol derivative or an alkylamino-NR'R" grouping, and each of R2 and R3 is independently a hydrogen atom or a grouping of formula (II), wherein each of R4 and R5 is independently a hydrogen atom or a grouping of formula (III), are disclosed. The corresponding pharmaceutical compositions, which are particularly useful in gene therapy for transferring therapeutic genes into cells, are also disclosed. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **182056-12-8P 182056-15-1P**
(preparation of compds. related to the amidinium family and their uses in gene therapy)
RN 182056-12-8 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

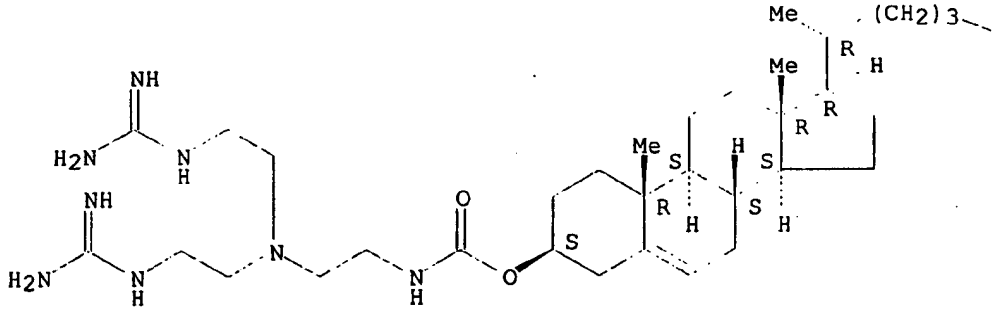


●2 HCl

RN 182056-15-1 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●2 HCl

PAGE 1-B

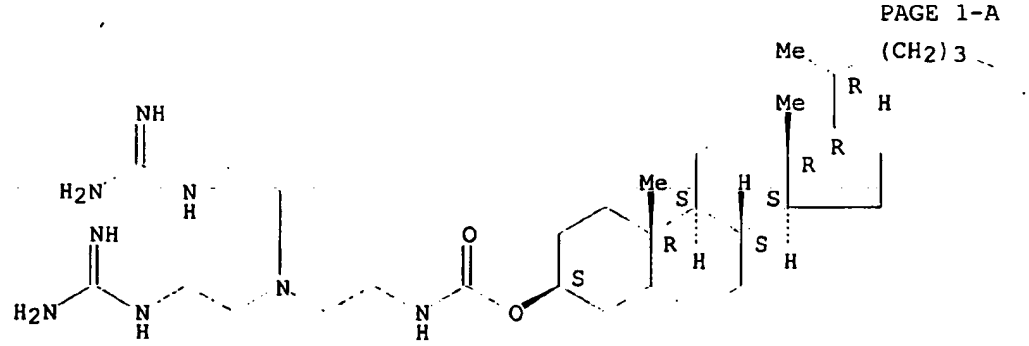
L35 ANSWER 3 OF 5 USPATFULL on STN
AN 2001:168815 USPATFULL
TI Alignment mechanism for computer system having a portable computer and

docking station
IN Helot, Jacques H., San Mateo, CA, United States
PA Hewlett-Packard Company, Palo Alto, CA, United States (U.S. corporation)
PI US 6297953 B1 20011002
AI US 1998-71052 19980430 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Picard, Leo P.; Assistant Examiner: Lea-Edmonds, Lisa
LREP Rose, Curtis G.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A computer system has a docking station and a portable computer. The docking station has a platform and a housing having a docking connector. The platform has one or more elevated rails. The portable computer has a computer connector, a base unit having a top portion and a bottom portion, a display unit connected to the top portion of said base unit, and one or more recessed grooves on the bottom portion of the base unit. The elevated rail or rails on the docking station interact with the recessed groove or grooves on the portable computer to guide the portable computer into a proper alignment with the housing of the docking station when the portable computer is placed on the platform and slid towards the housing so that the computer connector lines up with and connects to the docking connector. The docking station platform may have side walls or rotatable bumpers on the sides of the platform to provide coarse alignment between the docking station and the portable computer, and to prevent the portable computer from sliding off the platform during the alignment process. Preferably, the recessed groove or grooves are flared at the back edge of the portable computer to further assist in the alignment of the portable computer with the docking station. The docking station of the preferred and alternate embodiments of the invention can accommodate portable computers of different form factors and thus do not need to be replaced each time a new model of a personal computer is released with a different form factor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **182056-06-0**
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
RN 182056-06-0 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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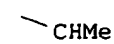
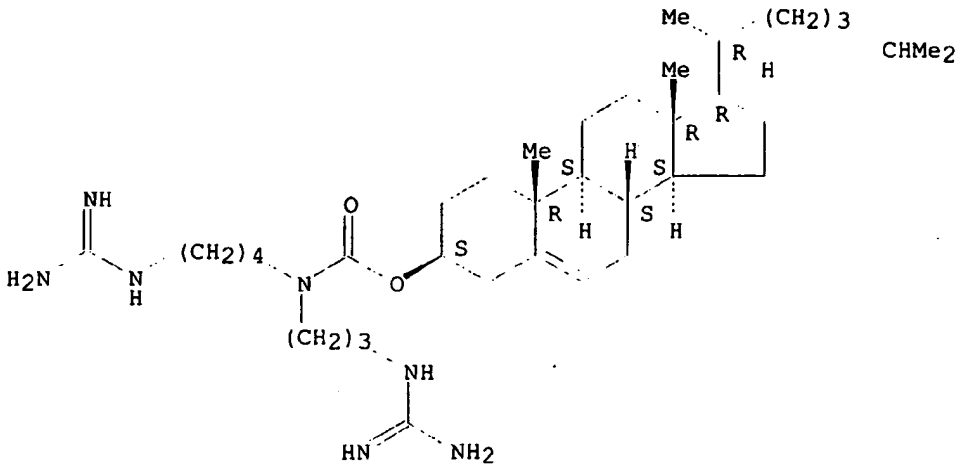


L35 ANSWER 4 OF 5 USPATFULL on STN
AN 2000:150149 USPATFULL
TI Compounds related to the amidinium family, pharmaceutical compositions containing same, and uses thereof
IN Lehn, Jean-Marie, Strasbourg, France
Lehn, Pierre, Paris, France
Vigneron, Jean-Pierre, Boissy-sur-Saint-Yon, France
PA Aventis Pharma S.A., Antony, France (non-U.S. corporation)
PI US 6143729 20001107
WO 9731935 19970904
AI US 1998-125825 19980911 (9)
WO 1997-FR364 19970228
19980911 PCT 371 date
19980911 PCT 102(e) date
PRAI FR 1996-2604 19960301
FR 1996-9557 19960730
DT Utility
FS Granted
EXNAM Primary Examiner: Elliott, George C.; Assistant Examiner: Epps, Janet
LREP Synnestvedt & Lechner LLP
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel amidinium derivatives of formula (I), wherein R1 is a cholesterol derivative or an alkylamino-NR'R" grouping, and each of R2 and R3 is independently a hydrogen atom or a grouping of formula (II), wherein each of R4 and R5 is independently a hydrogen atom or a grouping of formula (III), are disclosed. The corresponding pharmaceutical compositions, which are particularly useful in gene therapy for transferring therapeutic genes into cells, are also disclosed. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **182056-12-8P 182056-15-1P**
(preparation of compds. related to the amidinium family and their uses in gene therapy)
RN 182056-12-8 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

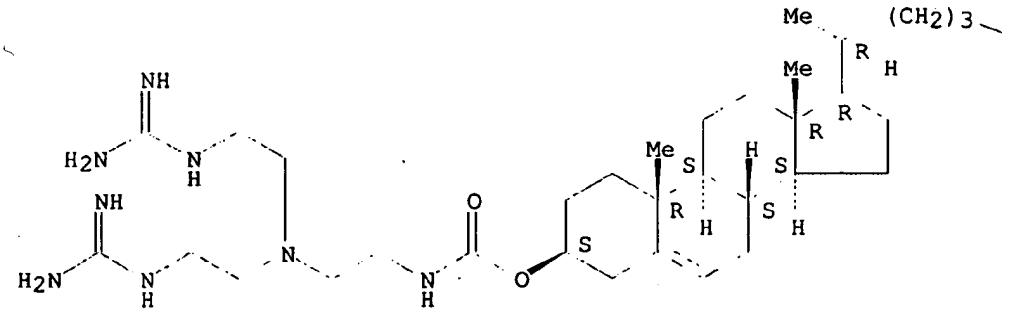


●2 HCl

RN 182056-15-1 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●2 HCl

PAGE 1-B

CHMe2

L35 ANSWER 5 OF 5 USPATFULL on STN
AN 2000:109365 USPATFULL
TI Stabilization of lipid:DNA formulations during nebulization
IN Densmore, Jr., Charles L., 83 S. Copper Sage Cr., The Woodlands, TX, United States 77381

Knight, J. Vernon, 29 Lana La., Houston, TX, United States 77027
Waldrep, J. Clifford, 6 Wind Trace Ct., The Woodlands, TX, United States 77381
Kinsey, Berma M., 3702 Elmore St., Houston, TX, United States 77005

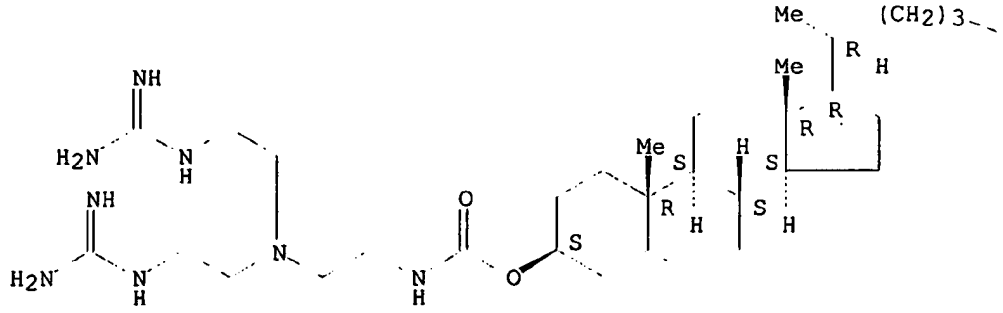
PI US 6106859 20000822
AI US 1999-227648 19990108 (9)
PRAI US 1998-71052P 19980108 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Schnizer, Richard
LREP Adler, Benjamin Aaron
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 475
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, (c) a neutral co-lipid; and (d) tryptone. Also provided is a nebulized cationic lipid:DNA suspension useful for lipid-DNA transfections, wherein said cationic lipid is bis(guanidinium)-tren-cholesterol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **182056-06-0**
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
RN 182056-06-0 USPATFULL
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

$-CHMe_2$

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:56:43 ON 08 DEC 2003

FILE COVERS 1907 - 8 Dec 2003 VOL 139 ISS 24
FILE LAST UPDATED: 7 Dec 2003 (20031207/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot l34

L34 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:399692 HCAPLUS
DN 139:255843
ED Entered STN: 27 May 2003
TI Gene therapy for hepatocellular carcinoma using non-viral vectors composed of bis guanidinium-tren-cholesterol and plasmids encoding the tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3
AU Tran, Phuong-Lan; Vigneron, Jean-Pierre; Pericat, David; Dubois, Sylvie; Cazals, Dominique; Hervy, Martial; DeClerck, Yves A.; Degott, Claude; Auclair, Christian
CS LBPA, CNRS-UMR 8532, Ecole Normale Superieure, Cachan, 94235, Fr.
SO Cancer Gene Therapy (2003), 10(6), 435-444
CODEN: CGTHEG; ISSN: 0929-1903
PB Nature Publishing Group
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 1, 14
AB Metalloproteinases (MMPs) and their natural inhibitors (TIMPs) contribute to the regulation of tumor microenvironment. Their expressions are deregulated in almost all human cancers. We report a novel approach to gene therapy of hepatocellular carcinoma (HCC), using repeated injections of DNA plasmids encoding the tissue inhibitors of metalloproteinases (TIMPs) TIMP-2 or TIMP-3, and a novel competent formulation of gene transfer based on nontoxic cationic cholesterol derivs. The new gene delivery system was efficient in demonstrating the antitumor efficiency of TIMP-2 or TIMP-3 in inhibiting tumor growth of human HuH7 HCC cells xenografted into nude mice. We show, for the first time, an in vivo effect of TIMP-3 in delaying HCC tumor growth. No treatment-related toxicity was noted. An inhibition of angiogenesis and tumor necrosis accompanied the inhibitory effects of TIMP-2 or TIMP-3 on tumor expansion and invasion. We also report a bystander effect produced by transfected HuH7 tumor cells mixed with untransfected cells in 1:1 ratio in culture that resulted in killing 98% of cells within 96 h. In addition, the soluble forms of TIMP-2 and TIMP-3 expressed by transfected cells exerted a cytotoxic effect on untransfected HuH7 cell cultures. Taken together, these results demonstrate the potential efficacy of repeated treatment of secreted TIMP-2 and TIMP-3 for the design of nonviral gene therapy for hepatocarcinoma.
ST gene therapy hepatocellular carcinoma lipoplex vector TIMP2 TIMP3; tissue inhibitor m talloproteinase gene therapy hepatocarcinoma; bis guanidinium tr n cholesterol lipoplex vector
IT Antitumor agents

Gene therapy
Plasmid vectors
(gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Human
Mouse
(gene therapy of human hepatocellular carcinoma xenografted in athymic mice)

IT Liver, neoplasm
(hepatoma; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Drug delivery systems
(liposomes; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT Transduction, genetic
(with BGTC vectors; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT 124861-55-8, Tissue inhibitor metalloproteinase-2 145809-21-8, Tissue inhibitor of metalloproteinase-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for; gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

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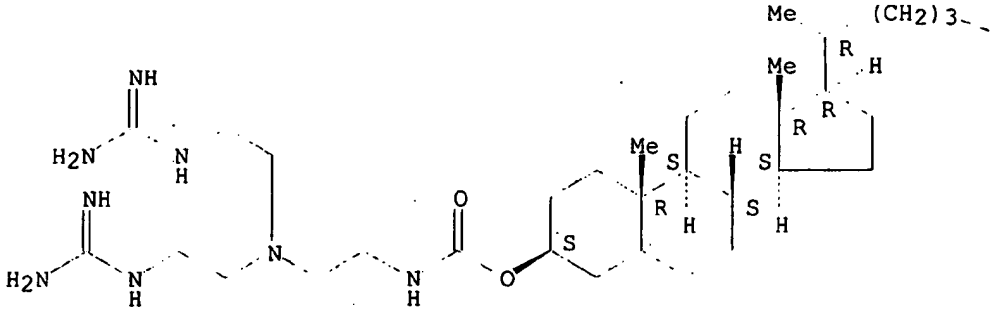
(44) Werb, Z; Cell 1997, V91, P439 HCAPLUS

IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene therapy for hepatocellular carcinoma using BGTC-DOPE lipoplex vectors and plasmids encoding tissue inhibitors of metalloproteinases TIMP-2 and TIMP-3)

RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe2

L34 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:311301 HCAPLUS
DN 137:389091
ED Entered STN: 25 Apr 2002
TI Various cationic carriers for in vitro transfection of tumor and endothelial cell lines
AU Zemlinska, Barbara; Sochanik, Aleksander; Missol-Kolka, Ewa; Szala, Stanislaw
CS Department of Molecular Biology, Center of Oncology-Maria Sklodowska-Curie Memorial Institute, Gliwice, 44-101, Pol.
SO Acta Biochimica Polonica (2002), 49(1), 285-290
CODEN: ABPLAF; ISSN: 0001-527X
PB Polish Biochemical Society
DT Journal

LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 3
AB We compared the efficiency of in vitro DNA transfer into selected tumor and endothelial cell lines using complexes of plasmid DNA and cationic carriers: DDAB/DOPE, DC-Chol/DOPE, Arg-Chol/DOPE, Gly-Chol/DOPE, Arg-Gly-Chol/DOPE, BGTC/DOPE, and PEI. The best carriers for transfecting the majority of tested cells lines at optimized carrier-to-DNA weight ratios were PEI and BGTC/DOPE.
ST tumor endothelium transfection plasmid DNA cationic carrier
IT Bladder, neoplasm
(carcinoma; cationic carriers for transfection of tumor and endothelial cell lines)
IT Genetic vectors
Human
Melanoma
Neoplasm
Plasmid vectors
Transformation, genetic
(cationic carriers for transfection of tumor and endothelial cell lines)
IT Blood vessel
(endothelium; cationic carriers for transfection of tumor and endothelial cell lines)
IT 3700-67-2, Dimethyldioctadecyl ammonium bromide 4004-05-1, DOPE 9002-98-6 73670-26-5 137056-72-5 **182056-06-0** 475645-85-3 475645-86-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic carriers for transfection of tumor and endothelial cell lines)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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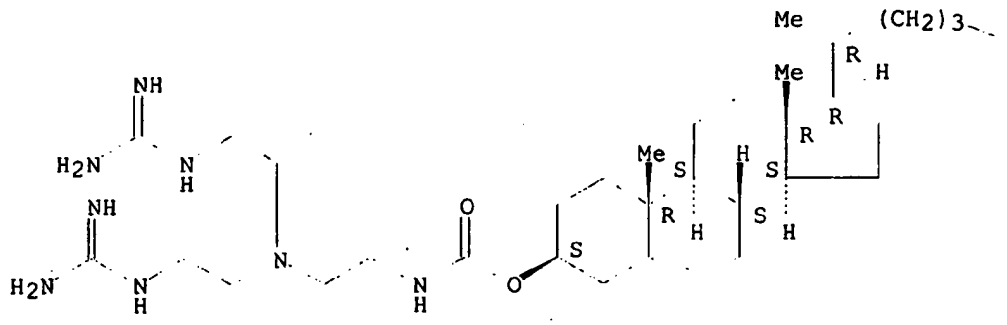
(21) Wicks, I; Hum Gene Ther 1995, V6, P317 HCAPLUS
IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic carriers for transfection of tumor and endothelial cell lines)
RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

$CHMe_2$

L34 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:309785 HCAPLUS
DN 136:319345
ED Entered STN: 25 Apr 2002
TI Stabilization of lipid:DNA formulations during nebulization
IN Densmore, Charles L., Jr.; Knight, J. Vernon; Waldrep, J. Clifford; Kinsey, Berma M.
PA Research Development Foundation, USA
SO U.S., 33 pp., Cont.-in-part of U.S. 6,106,859.
CODEN: USXXAM
DT Patent
LA English
IC ICM A16K009-127
ICS A16K051-00; C12N015-88
NCL 424450000
CC 1-1 (Pharmacology)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6375980	B1	20020423	US 1999-356635	19990719
	US 6106859	A	20000822	US 1999-227648	19990108
PRAI	US 1998-71052P	P	19980108		
	US 1999-227648	A2	19990108		

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, a neutral co-lipid; and tryptone. Also provided is a nebulized cationic lipid: neutral co-lipid: DNA suspension useful for lipid-DNA transfections, wherein the cationic lipid is bis(guanidinium)-tren-cholesterol and the neutral co-lipid is dioleoylphosphatidylethanolamine (DOPE).
ST liposome nebulization cationic neutral lipid tryptone DNA gene therapy
IT Gene, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TP53, gene therapy of lung cancer with; stabilization of lipid:DNA formulations during nebulization)
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic, liposomes containing; stabilization of lipid:DNA formulations during nebulization)

IT Cystic fibrosis
Lung, neoplasm
(gene therapy of; stabilization of lipid:DNA formulations during nebulization)
IT Phosphatidylcholines, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing egg yolk or hydrogenated soybean; stabilization of lipid:DNA formulations during nebulization)
IT Plasmid vectors
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)
IT Peptones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)
IT Drug delivery systems
(liposomes, aerosols; stabilization of lipid:DNA formulations during nebulization)
IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neutral, liposomes containing; stabilization of lipid:DNA formulations during nebulization)
IT Gene therapy
Transformation, genetic
(stabilization of lipid:DNA formulations during nebulization)
IT 63-89-8, Dipalmitoylphosphatidylcholine 4004-05-1, Dioleoylphosphatidylethanolamine 4235-95-4 18194-24-6, Dimyristoylphosphatidylcholine 18194-25-7, Dilauroylphosphatidylcholine **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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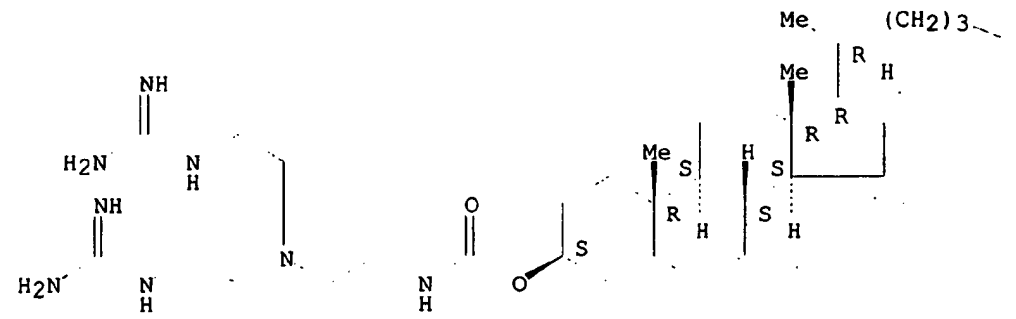
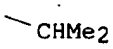
(2) Carr; US 5292746 A 1994 HCAPLUS
(3) Debs; US 5641662 A 1997 HCAPLUS
(4) Densmore; US 6106859 A 2000 HCAPLUS
(5) Unger; US 5469854 A 1995 HCAPLUS
(6) Vigneron; Proc Nat Acad Sci USA 1996, V93, P9682 HCAPLUS
(7) Yaroush; US 5077211 A 1991 HCAPLUS
IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing; stabilization of lipid:DNA formulations during nebulization)
RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L34 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:152502 HCAPLUS
DN 134:212794
ED Entered STN: 02 Mar 2001
TI Enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble molecule and anionic ligand for a cellular receptor.
IN **Nicolau, Yves Claude; Lehn, Jean-Marie**
PA **GMP Companies, Inc., USA**
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC 63-8 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001013933	A2	20010301	WO 2000-US22583	20000817
	WO 2001013933	A3	20010719		
	WO 2001013933	C2	20020912		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1223942	A2	20020724	EP 2000-957519	20000817
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003507430	T2	20030225	JP 2001-518070	20000817
PRAI	US 1999-150574P	P	19990825		
	WO 2000-US22583	W	20000817		

AB The present invention comprises compds., compns., and methods capable of delivering a broad range of anionic mols. to the cytoplasm of mammalian cells and methods that enhance the ability of mammalian red blood cells to deliver oxygen, by delivering a ligand for the allosteric site of Hb to

the cytoplasm of the blood cells. An example was given in which red blood cells were process with dodecasodium inositol hexaphosphate.

ST oxygen delivery Hb lipophilic ligand

IT Infection
(anaerobic; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cellular; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Alkalosis
Anemia (disease)
Hypoxia, animal
Lipophilicity
Lung, disease
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Sterols
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Hemoglobins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Heart, disease
(failure; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Necrosis
(gangrene; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Heart, disease
(infarction; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT Brain, disease
(stroke; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT **83-86-3**, Inositol hexaphosphate **17211-15-3**,
myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 57-88-5, Cholesterol, biological studies **182055-89-6**
182056-06-0
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT 7782-44-7, Oxygen, biological studi s
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

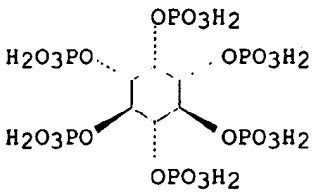
IT 57-12-5, Cyanide, biological studies 630-08-0, Carbon monoxide, biological studies 10102-43-9, Nitric oxide, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (poisoning; enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

IT **83-86-3**, Inositol hexaphosphate **17211-15-3**, myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

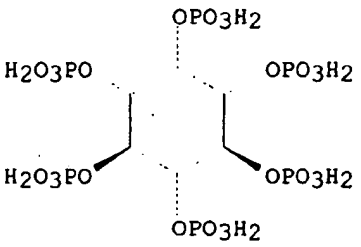
RN 83-86-3 HCAPLUS
CN myo-Inositol, hexakis(dihydrogen phosphate) (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 17211-15-3 HCAPLUS
CN myo-Inositol, hexakis(dihydrogen phosphate), dodecasodium salt (9CI) (CA INDEX NAME)

Relative stereochemistry.

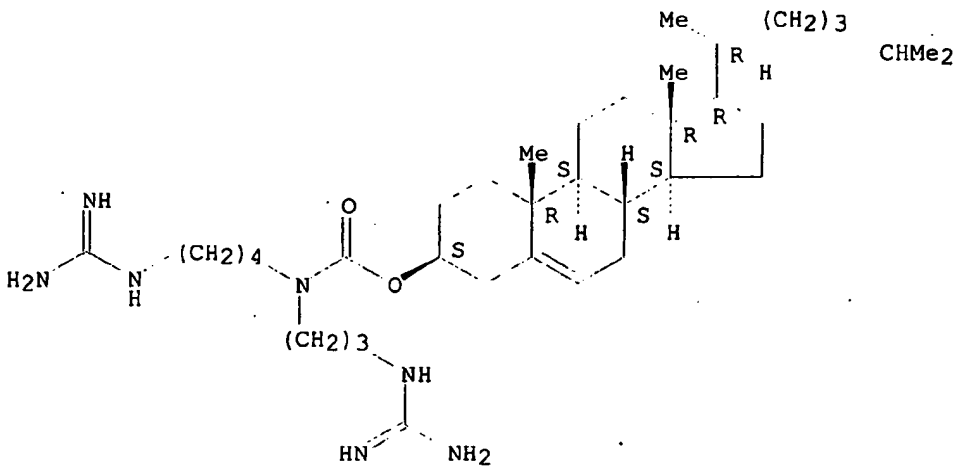


●12 Na

IT **182055-89-6 182056-06-0**
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhanced oxygen delivery in mammals comprising a cationic, lipophilic, water-soluble mol. and anionic ligand for a cellular receptor.)

RN 182055-89-6 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)

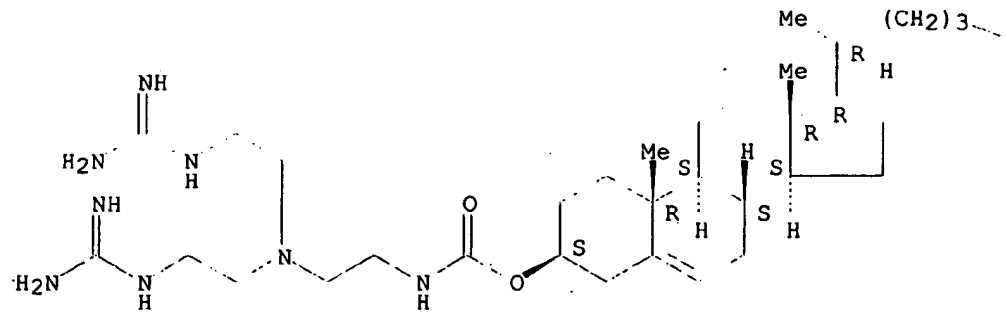
Absolute stereochemistry.



RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

L34 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:449397 HCAPLUS
DN 131:106801
ED Entered STN: 22 Jul 1999
TI Stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection
IN Densmore, Charles L.; Knight, J. Vernon; Waldrep, J. Clifford; Kinsey, Berma M.
PA Research Development Foundation, USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM A61K048-00
ICS C12N015-00; C12N005-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9934837	A1	19990715	WO 1999-US488	19990108
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	ZA 9900097	A	20000707	ZA 1999-97	19990107
	CA 2315708	AA	19990715	CA 1999-2315708	19990108
	AU 9923141	A1	19990726	AU 1999-23141	19990108
	AU 751969	B2	20020905		
	EP 1045703	A1	20001025	EP 1999-903023	19990108
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002500203	T2	20020108	JP 2000-527284	19990108
	RU 2213578	C2	20031010	RU 2000-120678	19990108
PRAI	US 1998-71052P	P	19980108		
	WO 1999-US488	W	19990108		

AB The present invention provides a liposomal aerosol composition, comprising a pharmaceutical compound, a cationic lipid, (c) a neutral co-lipid; and (d) tryptone. Also provided is a nebulized cationic lipid:DNA suspension useful for lipid-DNA transfections, wherein said cationic lipid is bis(guanidinium)-tren-cholesterol.

ST gene therapy transfection lipid DNA formulation

IT Peptones
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(Tryptones; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Lipids, biological studies
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cationic; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Drug delivery systems
(liposomes; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Promoter (genetic element)
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(of cytomegalovirus; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Cytomegalovirus
(promoter of; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Phosphatidylcholines, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(soya, hydrogenated; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Drug delivery systems
(sprays; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)

IT Animal tissue culture
Gene therapy
Genetic vectors
Plasmid vectors
Stabilizing agents
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT Phosphatidylcholines, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT DNA
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT Escherichia coli
(β-galactosidase reporter gene of; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT Reporter gene
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(β-galactosidase, of E. coli; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT 9031-11-2, β-Galactosidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reporter gene encoding, of E. coli; stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT 2462-63-7, Dioleoylphosphatidylethanolamine 2644-64-6, Dipalmitoylphosphatidylcholine 18656-38-7, Dimyristoylphosphatidylcholine 18656-40-1, Dilauroylphosphatidylcholine **182056-06-0**
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
IT 230949-32-3
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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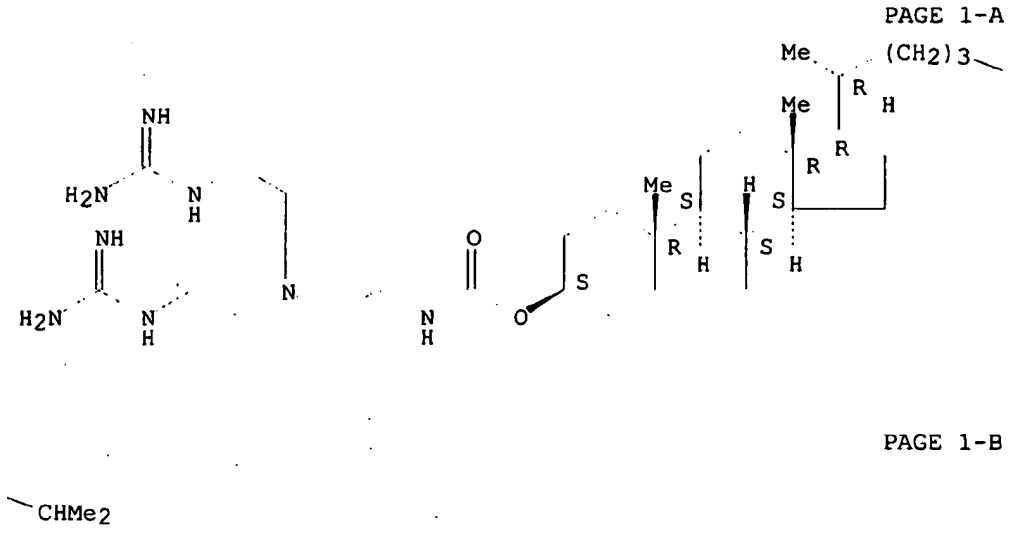
IT **182056-06-0**
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilization of lipid:DNA formulations during nebulization for gene-therapy transfection)
RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L34 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:198667 HCAPLUS
DN 131:54460
ED Entered STN: 29 Mar 1999
TI Structural characteristics of supramolecular assemblies formed by guanidinium-cholesterol reagents for gene transfection
AU Pitard, Bruno; Oudrhiri, Noufissa; Vigneron, Jean-Pierre; Hauchecorne, Michelle; Aguerre, Olivier; Toury, Renee; Airiau, Marc; Ramasawmy, Rajen; Scherman, Daniel; Crouzet, Joel; **Lehn, Jean-Marie**; Lehn, Pierre
CS Unite Mixte de Recherche, 133 Rhone-Poulenc Rorer, Centre National de la Recherche Scientifique, Vitry-sur-Seine, 94403, Fr.
SO Proceedings of the National Academy of Sciences of the United States of America (1999), 96(6), 2621-2626
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 9
AB We have recently discovered that cationic cholesterol derivs. characterized by guanidinium polar headgroups are very efficient for gene transfection in vitro and in vivo. In spite of being based on some rationale at the mol. level, the development of these new synthetic vectors was nevertheless empirical. Indeed, the factors and processes underlying cationic lipid-mediated gene transfer are still poorly understood. Thus, to get a better insight into the mechanisms involved, we have examined the supramol. structure of lipid/DNA aggregates obtained when using reagent bis(guanidinium)-tren-cholesterol (BGTC), either alone or as a liposomal formulation with the neutral phospholipid dioleoyl phosphatidylethanolamine (DOPE). We here report the results of cryotransmission electron microscopy studies and small-angle x-ray scattering expts., indicating the presence of multilamellar domains with a regular spacing of 70 Å and 68 Å in BGTC/DOPE-DNA and BGTC-DNA aggregates, resp. In addition, DNA lipoplexes with similar lamellar patterns were d tected inside transfected HeLa cells by conv ntional transmission electron microscopy. Thes results suggest that DNA condensation by multivalent guanidinium-cholesterol cationic lipids involves the formation of highly ordered multilamellar domains, the DNA mols. being intercalated between the lipid bilayers. These results also invite further

investigation of the intracellular fate of the internaliz d lipid/DNA structures during their trafficking toward the cell nucleus. The identification of the basic features of active complexes should indeed help in the design of improved guanidinium-based vectors.

ST supramol assembly structure guanidinium cholesterol reagent transfection

IT HeLa cell
(DNA lipoplexes with lamellar patterns detected inside transfected HeLa cells; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT DNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(condensation, by guanidinium-cholesterol cationic lipids involves formation of highly ordered multilamellar domains; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT Drug delivery systems
(liposomes, structure of lipid/DNA aggregates in; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT 2462-63-7, Dioleoyl phosphatidylethanolamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bis(guanidinium)-tren-cholesterol with, in liposome; structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

IT **182056-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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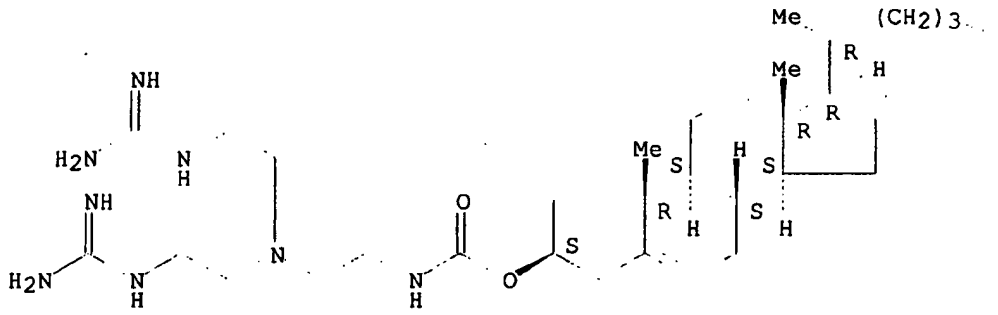
IT **182056-06-0**
RL: BAC (Biological activity or effector, xcept adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structural characteristics of supramol. assemblies formed by guanidinium-cholesterol reagents for gene transfection)

RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

L34 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:687119 HCAPLUS
DN 130:57047
ED Entered STN: 30 Oct 1998
TI Guanidinium-cholesterol cationic lipids: novel reagents for gene transfection and perspectives for gene therapy
AU Oudrhiri, N.; Vigneron, J. P.; Hauchecorne, M.; Toury, R.; Lemoine, A. I.; Peuchmaur, M.; Navarro, J.; **Lehn, J. M.**; Lehn, P.
CS Hopital Robert Debre, INSERM U.458, Paris, 75019, Fr.
SO Biogenic Amines (1998), 14(5), 537-552
CODEN: BIAME7; ISSN: 0168-8561
PB VSP BV
DT Journal; General Review
LA English
CC 63-0 (Pharmaceuticals)
Section cross-reference(s): 1, 3
AB A review with refs. Artificial self-assembling systems are at present widely investigated as an alternative approach to recombinant viruses for gene transfer studies and gene therapy applications. Among these synthetic vectors, cationic lipids are particularly attractive as it is possible to design and synthesize a great variety of reagents. Several amine-carrying cationic lipids have been shown to be efficient for gene transfection; moreover, some reagents (DC-Chol:DOPE, DOTAP...) have even already been used in clin. trials. Over the last years, we have developed a novel class of cationic lipids : cholesterol derivs. characterized by polar head groups containing guanidinium functions. Such reagents combine the membrane compatible features of the cholesterol subunit and the favorable features of the guanidinium groups for DNA binding. We herein intend to summarize our work showing that these novel cationic lipids are efficient for gene transfection in vitro (into various mammalian cell lines and primary human airway c lls) and also in vivo (into the mouse airway epithelium). These studies confirm the potential of cationic lipids for human gene therapy, namely lung-directed gene therapy for Cystic Fibrosis. Most importantly, our work also provides the basis for the design of

improved artificial gene delivery systems. Thus, in this forward-looking review, we will also discuss some of the remaining problems that need to be resolved in order to develop improved synthetic vectors for nonviral gene delivery.

ST review

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic; guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

IT Drug delivery systems
Gene therapy
Transformation, genetic
(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

IT **182056-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD

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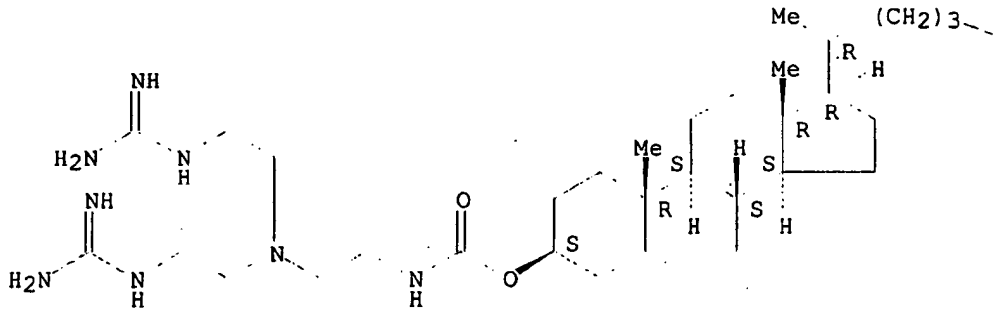
IT **182056-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guanidinium-cholesterol cationic lipids for gene transfection and perspectives for gene therapy)

RN 182056-06-0 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe2

L34 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:594745 HCAPLUS
DN 127:234484
ED Entered STN: 17 Sep 1997
TI Preparation of compounds related to the amidinium family and their uses in gene therapy
IN **Lehn, Jean-Marie**; Lehn, Pierre; Vigneron, Jean-Pierre
PA Centre National de la Recherche Scientifique, Fr.; Lehn, Jean-Marie; Lehn, Pierre; Vigneron, Jean-Pierre
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM C07J041-00
ICS A61K031-575; A61K009-127; C12N015-88
CC 32-7 (Steroids)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9731935	A1	19970904	WO 1997-FR364	19970228

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO,

SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

FR 2745569	A1	19970905	FR 1996-2604	19960301	
FR 2745569	B1	19980507			
FR 2751972	A1	19980206	FR 1996-9557	19960730	
FR 2751972	B1	19980904			
CA 2248186	AA	19970904	CA 1997-2248186	19970228	
AU 9719304	A1	19970916	AU 1997-19304	19970228	
AU 723998	B2	20000907			
EP 888379	A1	19990107	EP 1997-907154	19970228	
EP 888379	B1	20010110			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI

BR 9707889	A	20000104	BR 1997-7889	19970228	
JP 2000506136	T2	20000523	JP 1997-530677	19970228	
AT 198599	E	20010115	AT 1997-907154	19970228	
ES 2154453	T3	20010401	ES 1997-907154	19970228	
PT 888379	T	20010531	PT 1997-97907154	19970228	
NO 9803691	A	19980812	NO 1998-3691	19980812	
US 6143729	A	20001107	US 1998-125825	19980911	
US 6316422	B1	20011113	US 2000-706619	20001106	
PRAI FR 1996-2604	A	19960301			
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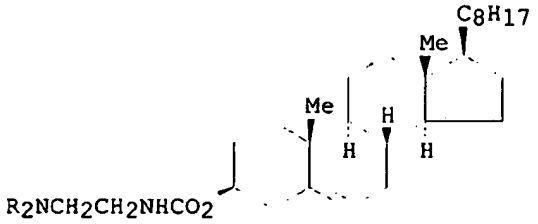
WO 1997-FR364	W	19970228			
US 1998-125825	A1	19980911			

GI



I

AB Novel amidinium derivs. R2R3NCO2R1 [R1 = cholesterol derivative, alkylamino group; R2, R3 = H, {(CH2)nNR4}mR5; R4, R5 = H, (CH2)p(X)r{(CH2)qC(NH2):N+H2}x] are disclosed. Amidine salt I·2HCl [R = (CH2)2NHC(NH2):NH] was prepd, from cholesterol chloroformate via sequential addition of tris(2-aminoethyl)amine and 1H-pyrazole-1-carboximidine. I is useful in gene therapy for transferring therapeutic genes into cells as shown by the expression of luciferase in human A549 cells (4x105 RLU/mg), in monkey COS-7 cells (2.1x107 RLU/mg), in dog MDCK-1 cells (3x106 RLU/mg) and in rat ROS cells (4x106 RLU/mg).

ST steroid amidinium deriv prepn gene therapy; cholesterol amidinium deriv prepn gene therapy

IT Amidines
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(cationic; preparation of compds. related to the amidinium family and their uses in gene therapy)

IT Gene therapy
(preparation of compds. related to the amidinium family and their uses in

gene therapy)

IT Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

IT Liposomes
Micelles
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy in)

IT DNA
Plasmids
RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy with)

IT **182056-12-8P 182056-15-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

IT 9014-00-0, Luciferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

IT 111-94-4, Iminobis(propionitrile) 2462-63-7, Dioleoylphosphatidylethanolamine 4023-02-3, 1H-Pyrazole-1-carboxamidine hydrochloride 4097-89-6, TREN 7144-08-3, Cholesterol chloroformate 83392-10-3, N1,N8-Di(tert-butoxycarbonyl)spermidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

IT 179075-25-3P 195253-95-3P 195253-96-4P 195253-97-5P 195253-98-6P 195253-99-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

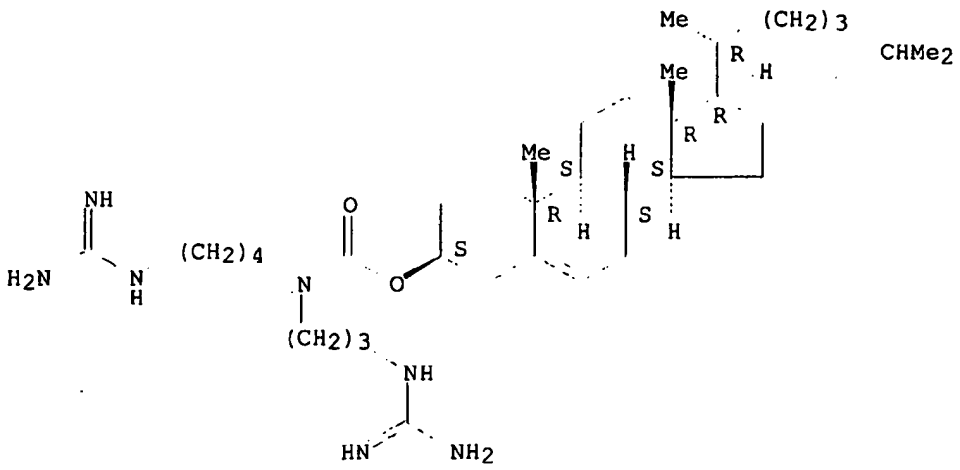
IT 195254-00-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

IT **182056-12-8P 182056-15-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of compds. related to the amidinium family and their uses in gene therapy)

RN 182056-12-8 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

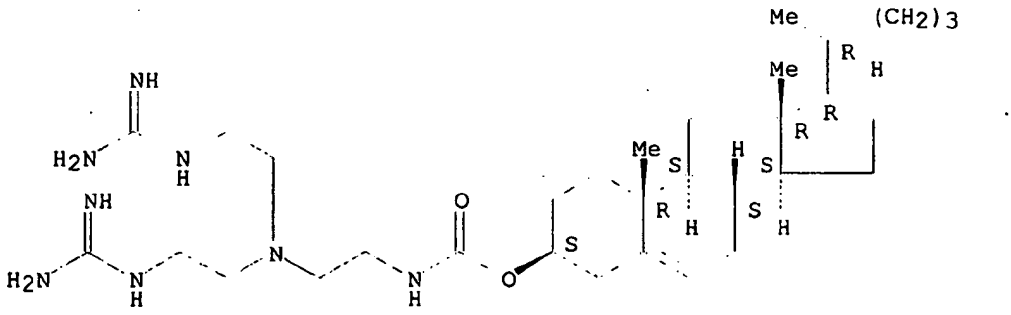


●2 HCl

RN 182056-15-1 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



●2 HCl

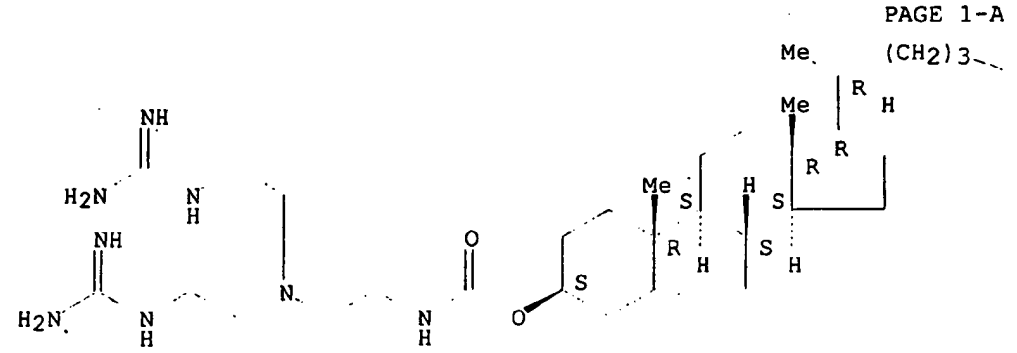
PAGE 1-B

L34 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:172669 HCAPLUS
DN 126:258428
ED Entered STN: 14 Mar 1997
TI Gene transfer by guanidinium-cholesterol cationic lipids into airway

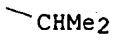
epithelial cells in vitro and in vivo
AU Oudrhiri, Noufissa; Vigneron, Jean-Pierre; Peuchmaur, Michel; Leclerc, Tony; **Lehn, Jean-Maire**; Lehn, Pierre
CS Inst. Natl. Sante Recherche Medicale, Hopital Robert Debre, Paris, 75019, Fr.
SO Proceedings of the National Academy of Sciences of the United States of America (1997), 94(5), 1651-1656
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 1-2 (Pharmacology)
Section cross-reference(s): 63
AB Synthetic vectors represent an attractive alternative approach to viral vectors for gene transfer, in particular into airway epithelial cells for lung-directed gene therapy for cystic fibrosis. Having recently found that guanidinium-cholesterol cationic lipids re efficient reagents for gene transfer into mammalian cell lines in vitro, the authors have investigated their use for gene delivery into primary airway epithelial cells in vitro and in vivo. The results obtained indicate that the lipid bis(guanidinium)-tren-cholesterol (BGTC) can be used to transfer a reporter gene into primary human airway epithelial cells in culture. Furthermore, liposomes composed of BGTC and dioleoyl phosphatidylethanolamine (DOPE) are efficient for gene delivery to the mouse airway epithelium in vivo. Transfected cells were detected both in the surface epithelium and in submucosal glands. In addition, the transfection efficiency of BGTC/DOPE liposomes in vitro was quant. assessed by using the luciferase reporter gene system.
ST gene transfer cationic lipid airway epithelium
IT Respiratory tract
(epithelium; gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
IT Gene therapy
Genetic vectors
Transduction, genetic
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
IT Drug delivery systems
(liposomes; gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into airway epithelial cells in vitro and in vivo)
IT 4004-05-1, Dioleoyl phosphatidylethanolamine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into human and laboratory animal airway epithelial cells in vitro and in vivo)
IT **182056-06-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene transfer by guanidinium-cholesterol cationic lipids in liposomes into airway epithelial cells in vitro and in vivo)
RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolut stereoch mistry.

PAGE 1-A



PAGE 1-B



L34 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:553205 HCAPLUS
DN 125:239451
ED Entered STN: 17 Sep 1996
TI Guanidinium-cholesterol cationic lipids: efficient vectors for the transfection of eukaryotic cells
AU Vigneron, Jean-Pierre; Oudrhiri, Noufissa; Fauquet, Mireille; Vergely, Laurence; Bradly, Jean-Claude; Basseville, Monique; Lehn, Pierre; **Lehn, Jean-Marie**
CS Laboratoire de Chimie des Interactions Moleculaires, College de France, Paris, 75005, Fr.
SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(18), 9682-9686
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 6
AB Two cationic lipids, bis-guanidinium-spermidine-cholesterol(BGSC) and bis-guanidinium-tren-cholesterol (BGTC)-cholesterol derivs. bearing two guanidinium groups-have been synthesized and tested as artificial vectors for gene transfer. They combine the membrane compatible features of the cholesterol subunit and the favorable structural and high pKa features of the guanidinium functions for binding DNA via its phosphate groups. Reagent BGTC is very efficient for transfection into a variety of mammalian cell lines when used as a micellar solution In addition, both BGTC and BGSC present also a high transfection activity when formulated as liposomes with the neutral phospholipid dioleoylphosphatidyl ethanolamine. These results reveal the usefulness of cholesterol derivs. bearing guanidinium groups for gene transfer.
ST guanidinium cholesterol genetic vector transformation eukaryote
IT Eukaryote
Genetic vectors
Liposome
Transformation, genetic
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)
IT 57-88-5D, Cholesterol, guanidinium derivs.

RL: BPR (Biological process); BSU (Biological study, unclassifi d); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process); USES (Uses)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

IT 2462-63-7
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

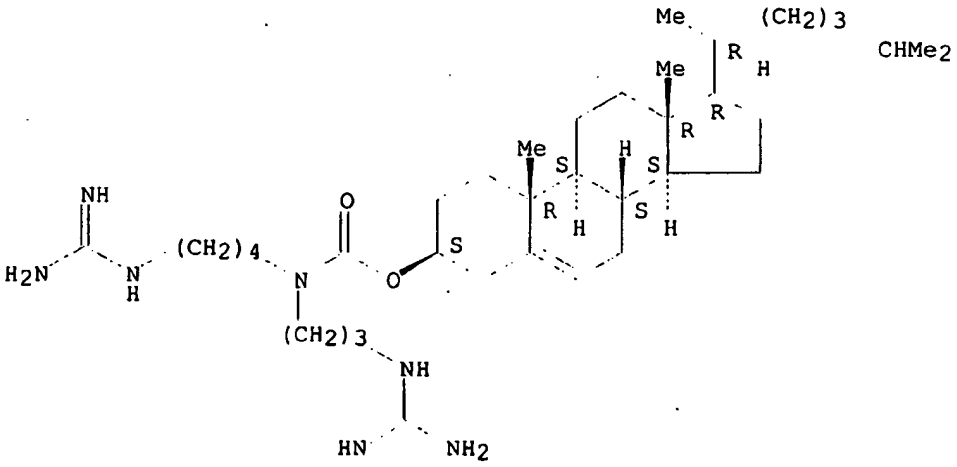
IT **182055-89-6P 182056-06-0P 182056-12-8P**
182056-15-1P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

IT 4023-02-3 4097-89-6 7144-08-3 83392-10-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

IT **182055-89-6P 182056-06-0P 182056-12-8P**
182056-15-1P
RL: BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(guanidinium-cholesterol cationic lipids as efficient vectors for the transfection of eukaryotic cells)

RN 182055-89-6 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate (9CI) (CA INDEX NAME)

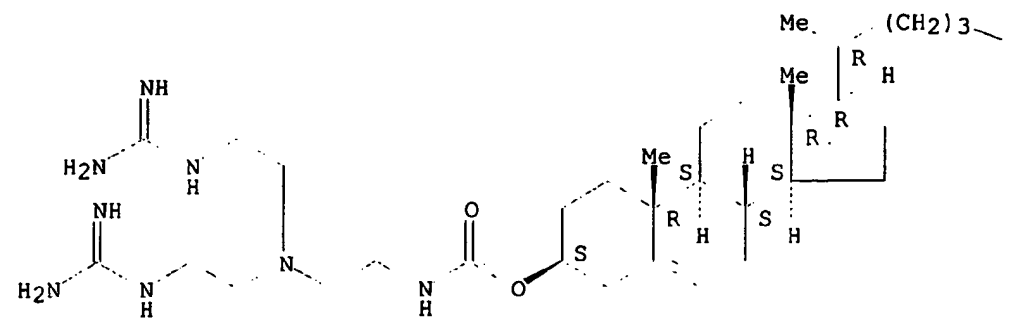
Absolute stereochemistry.



RN 182056-06-0 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

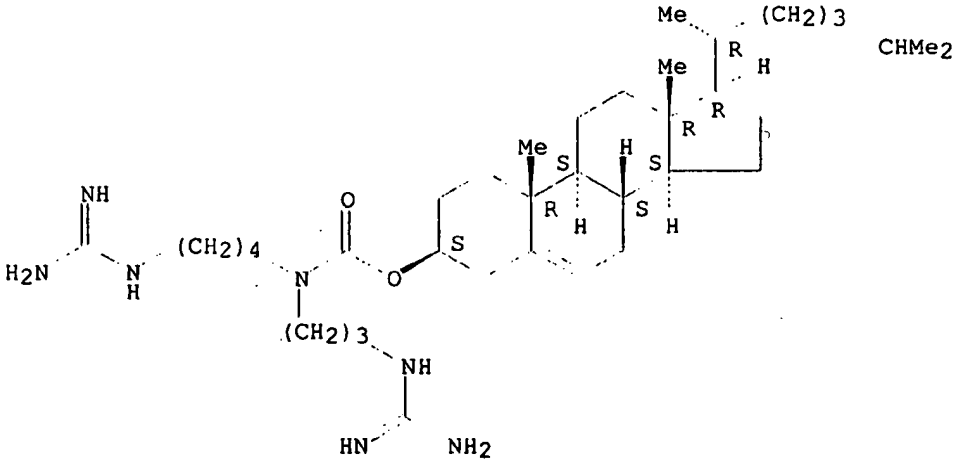
PAGE 1-A



PAGE 1-B

RN 182056-12-8 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [4-[(aminoiminomethyl)amino]butyl][3-[(aminoiminomethyl)amino]propyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

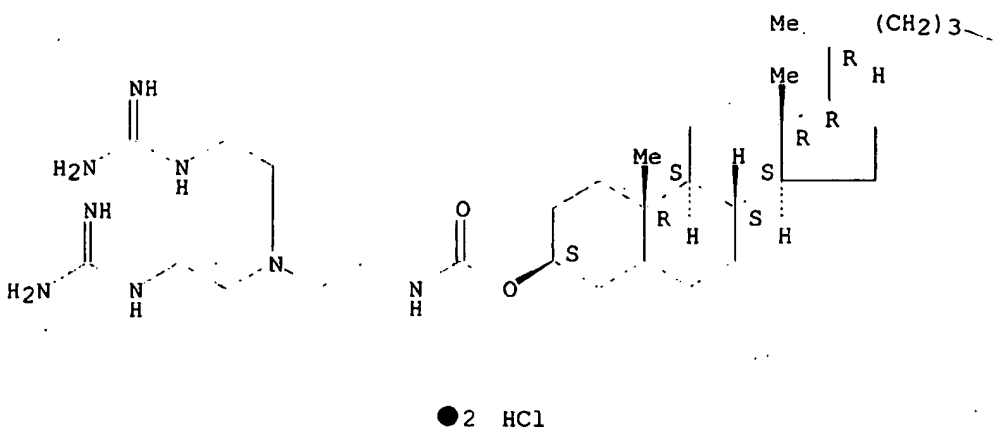


●2 HCl

RN 182056-15-1 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, [2-[bis[2-[(aminoiminomethyl)amino]ethyl]amino]ethyl]carbamate, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



● 2 HCl

PAGE 1-B

CHMe2

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